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Pubertal Weight Gain in Female Rhesus Macaques

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ABSTRACT In order to describe the timing and extent of accelerated pubertal weight gain in female rhesus, we examined a large colony data base consisting of over 10,000 weight records for animals between 1.5 and 3.0 years of age (menarche occurs at about 2.6 years). Average colony weights were determined by week of age from information on age at weighing. Cross-sectional analyses with linear regression demonstrated an acceleration in weight increase from 196 to 231 weeks (28–33 months) when colony weights increased 381 g/12 weeks as opposed to an average of 193 and 203 g, respectively, during the preceding and succeeding age intervals of the same length. Longitudinal analyses (n = 428) indicated that maximum individual growth velocity averaged 499 ± 18 g/12 weeks and occurred at 119 ± 5.6 weeks (29.7 ± 0.2 months) of age. Nonlinear modeling with the Gompertz function indicated that decelerating growth rates seen at earlier ages were not characteristic of the period of accelerated pubertal growth.

Humans and other primate species experience a period of rapid linear and ponderal growth preceding the onset of fertility and the completion of epiphyseal closure (Tanner and Whitehouse, 1976; Watts and Gavan, 1982). Rhesus macaques have been the most widely studied nonhuman primate species in this regard, primarily as a biomedical model for human sexual maturation (Terasawa et al., 1983; Perera and Plant, 1992). The available data indicate that rhesus females begin pubertal hormonal changes at about 21 months of age, reach menarche at 31 months of age, and first ovulate at 48 months of age (Terasawa et al., 1983). Estimates of the timing and extent of the period of accelerated growth in the pubertal female rhesus vary considerably and have been derived primarily from relatively small populations (<100) maintained for research projects (Goy et al., 1983; Kemnitz, 1984; Wilson et al., 1984; Tanner et al., 1990). Notably, few quantitative analyses of changes in growth rate during the pubertal period have been undertaken. Laird (1967) has noted that the exponential decrease in weight growth rate (Gompertz function) characteristic of lifespan growth in nonprimate species does not apply to adolescent growth of humans. Watts and Gavan (1982) were able to fit a single exponential growth curve to limb size data of rhesus monkeys from birth to 5 years of age; however, positive deviations from the predicted sizes were consistently seen during adolescence. German et al. (1994) applied an exponential growth model to weight data from pigtailed macaques (*Macaca nemestrina*) aged 0–10 years and found that a biphasic model was required to accommodate growth spurts occurring in infancy and adolescence. Also, separate models were required for males and females.

In the current study, we examined a large data base of body weights collected for

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colony management purposes. Young monkeys have minimal body fat at this age, so that body weight changes are a good surrogate for general somatic growth. Using this population, we attempted to develop further information concerning pubertal growth rates in female monkeys using linear and nonlinear modeling.

MATERIALS AND METHODS

The original data base consisted of 10,830 weights of 2,586 female rhesus monkeys (*Macaca mulatta*) 1.5–3.0 years of age that had been entered into a computerized system during routine colony management. Later ages could not be used because pregnancies began to occur. The monkeys were maintained at the California Primate Research Center at the University of California, Davis between 1987 and 1991. Animals in this age range were typically housed outdoors in field cages (61 m × 30.5 m × 2.44 m) with 80–90 males and females per cage, or in corn cribs (4.27 m × 14.03 m) with 12–20 males and females per cage. Climbing and playing apparatus were in both types of enclosure. Twenty-eight point nine percent of the recorded weights were taken from monkeys that were housed, at the time that individual weight was obtained, indoors in temperature- (68°–72°F) and light- (12 hr on, 12 hr off) controlled rooms. Water was provided ad libitum via an automatic water system. Diet for all animals consisted of Purina Monkey Chow.

Weights were typically obtained at 3 month intervals or whenever an animal was moved or treated by veterinarians. Weights were obtained with scales accurate to at least the nearest 100 g. The computer contained birthdates and provided age in days at the time of weighing based on the date. To provide standardized ages for comparison, weights for which age in days fell within a 1 week (7 day) period were grouped together. Age in months was determined by dividing by 4.

The original data base was edited by deleting weights under a number of circumstances. Monkeys listed under any project code involving SAIDS (Simian Acquired Immunodeficiency Syndrome, a model for human AIDS) were deleted from the data base (27%). In addition, all recorded weights within 30 days before any monkey's death were deleted (2%). Any weight after 2 years of age was deleted for any females that conceived before 3 years of age (3%). Two biologically improbable weights were deleted. When more than one weight was recorded in a 1 week (7 day) time period for a particular monkey, the first weight was kept and the remaining weights for that week were deleted (~4%). The final data base contained an average of 83 (range 57–114) weights of different monkeys per week.

To determine colony weight gain rates (cross-sectional analysis), mean and 95% confidence intervals were first obtained independently for each weekly interval. Linear regression was conducted across ages using the mean weekly values at successive 3, 4, 5, and 6 months intervals in order to determine the optimal age ranges to detect changes in rate of weight gain. Weight gain was expressed as grams/12 weeks because this was the minimal period for which linear estimates of weight change (linear regressions) could be successfully fitted. Calculations utilized Excel 2.2, Statview 512+, and SAS version 4.0 software. Nonlinear modeling was conducted with the NLIN procedure of SAS using the Marquardt method for obtaining a least-squares fit to a Gompertz equation ($W = l/k*1 - \exp(-k*a)$), where W = weight at age "a," a = age in months, 1 = initial growth rate, and k = rate of exponential decline in the initial growth rate].

To study weight gain patterns of individuals, a subset of 442 animals was selected for whom 4–6 weights had been recorded from 18 to 36 months of age. If more than one of these weights was taken at an interval of less than 12 weeks, the record was excluded. In addition, records were excluded for animals that gained or lost more than 1,000 grams/12 weeks, indicating either an inaccurate weight or a sick animal. Weight gain velocity was calculated as the difference in weight at two successive weighings divided by the difference in age. A corresponding age for each weight gain velocity measurement was calculated as the midpoint between the weighings used to compute weight gain. Peak weight gain velocity (in terms of grams/

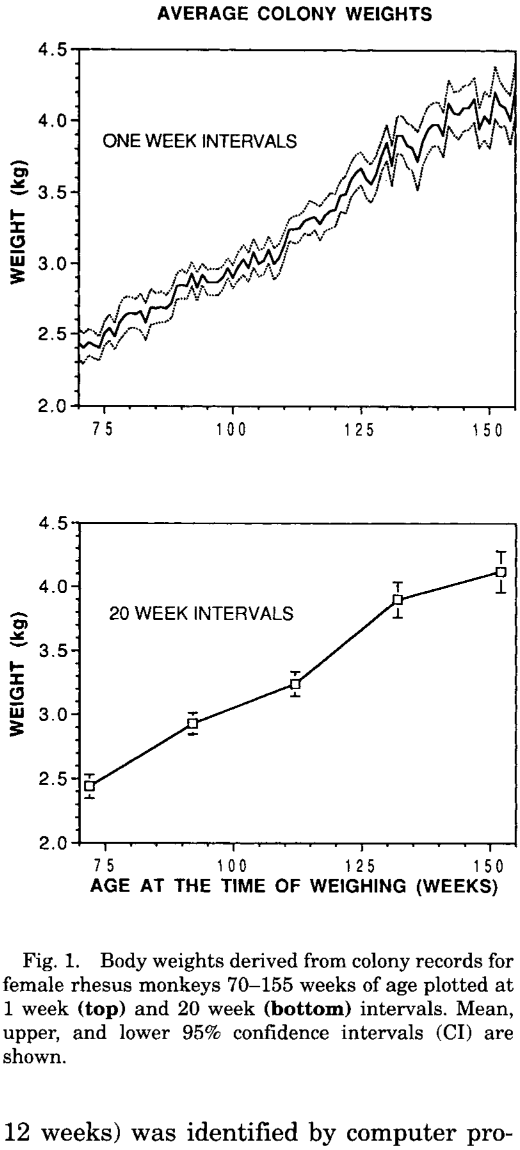

Fig. 1. Body weights derived from colony records for female rhesus monkeys 70–155 weeks of age plotted at 1 week (**top**) and 20 week (**bottom**) intervals. Mean, upper, and lower 95% confidence intervals (CI) are shown.

12 weeks) was identified by computer program and other weights were ordered relative to this age. Calculations utilized SAS 4.0 statistical software.

RESULTS

In Figure 1, weights are plotted by 1 and 20 week intervals from 70 to 155 weeks of age. The plot demonstrated that patterns of weight increase are not discernible from the weekly data but are more apparent at the longer interval, which was selected for quantitative analysis as described below.

Weight change velocities (slopes of the regressions) at intervals of 3, 4, and 5 months are plotted in Figure 2. Changes in rate of weight gain were most distinct when linear regressions were fitted at 5 month intervals. Weight change from 28 to 33 months (midpoint of interval, 122 weeks) was significantly greater than from 23 to 28 or 33 to 38 months, as indicated by the lack of overlap of the 95% CI for the slopes at successive age periods. Significant linear regressions could not be fitted at 2 month intervals and all slopes overlapped at 6 month intervals.

Composite individual growth velocity curves are plotted in Figure 3. The peak weight velocity of 499 ± 18 g/12 weeks occurred on the average at 119 ± 5.6 weeks (29.7 ± 0.2 months) of age when weight gain was a little over twice as rapid as at the pre- and postpeak weighings.

Nonlinear modeling with the Gompertz function was conducted for time periods from 18 to 28 months of age (10 months prior to the period of accelerated pubertal growth) and from 28 to 37 months of age (including the growth spurt and subsequent 5 month period). Adequate fit as determined by least-squares estimates was obtained for both time periods. The initial growth rate (l) and exponential decrease in growth rate (k) were 197 g/month and 46 g/month, respectively, prior to initiation of the period of accelerated growth, and 130 g/month and 8 g/month after initiation of the period of accelerated growth. Comparison of the values for k indicate that deceleration in growth rate is markedly reduced after initiation of accelerated pubertal weight gain.

DISCUSSION

Estimates of the timing and extent of peak weight gain rates in pubertal female rhesus vary considerably across studies. Wilen and Naftolin (1976) identified the peak in pubertal weight gain in six animals shortly after menarche (1.9 years, 24.8 months of age). Foster (1977) identified peak weight gain velocity in four animals at 25–36 months of age. Tanner et al. (1990) identified peak weight gain velocities for animals housed indoors from 23 to 26 months (nine animals), a first peak for six outdoor monkeys at 23–26 months (two monkeys) and a second peak at 26–29 months (four monkeys) (weights were

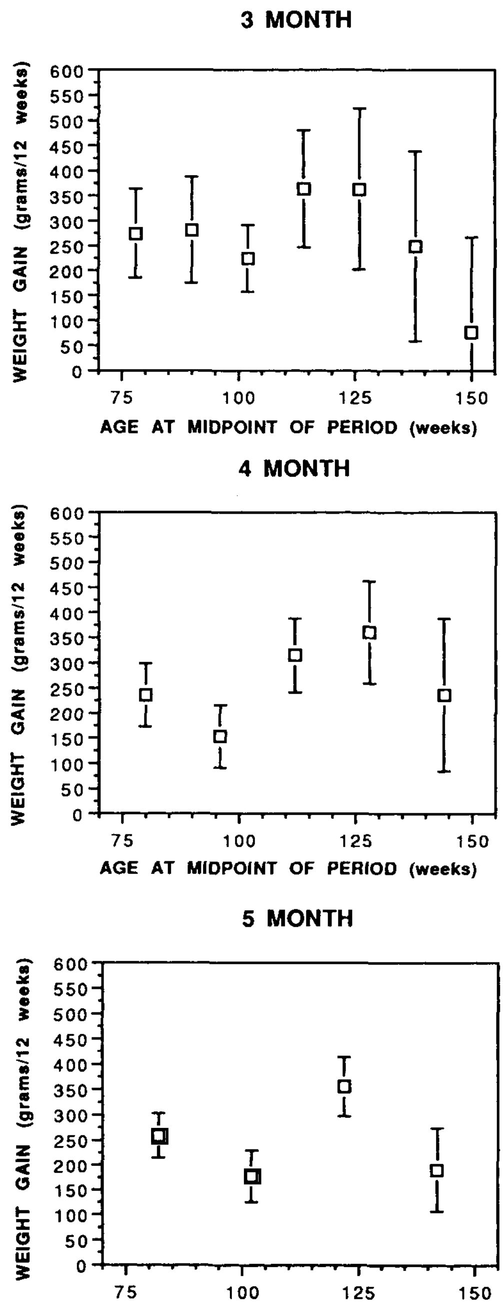

Fig. 2. Weight gain velocity (slope of regression) determined by fitting linear regressions to weekly weight data at 3, 4, and 5 month intervals. Upper and lower 95% CI are also shown. Slope values whose 95% CIs do not overlap are significantly different by heterogeneity of slope tests.

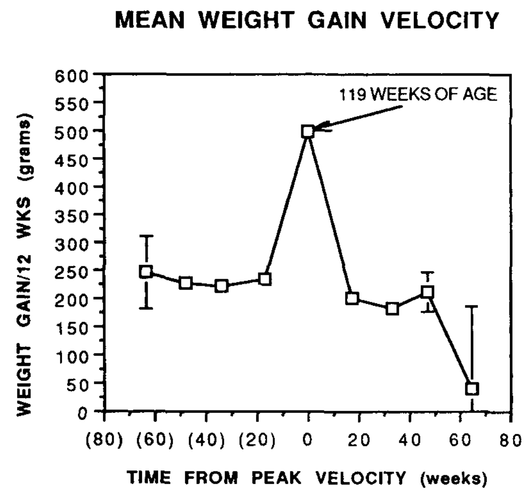

Fig. 3. Peak weight gain velocity derived from averaging weight gain velocity curves of 428 individual animals. Mean ± SEM of individual weight gains are shown. Pre- and postpeak velocities are also shown. It should be noted that any individual animal had a maximum of six weights available so that no animal is represented at all pre- and postpeak time points. The peak weight gain velocity occurred on the average at 832 days of age (119 weeks, 29.7 4-week months, 27.7 30-day months, 2.28 years).

reported at 3 month intervals). Wilson et al. (1984) showed an increasing percentage of change in body weight for 77 female rhesus monkeys from 29 to 40 months of age. The authors identify an 8.7% body weight change from 29 to 34 months and a 34.3% body weight change from 35 to 40 months, considerably later than in our study. Terasawa et al. (1983) describe a period of accelerated growth from 18 to 31 months of age (prior to menarche) and from 38 to 47 months of age (prior to first ovulation) in 37 female rhesus. Goy et al. (1983) identified a pubertal growth surge peaking at 31 months in a sample of 86 females. This is similar to the 29.7 month time for peak weight gain velocity in the present study. Van Wagenen and Catchpole (1956) found that weight gain of premenarchial rhesus females peaked at 140 g/month at 2.5 years of age. This peak weight gain is also very similar to our colony data in extent (127 g/month) and timing (2.3 years).

The present study has the advantage of a large data base containing animals from a variety of genetic and rearing backgrounds,

thus helping to establish the generality of findings from studies with smaller samples and homogeneous housing conditions. Further, ascertainment of accelerated weight gain in other studies has been determined by examination of patterns of plotted data without quantitative analysis. In this study, linear regression was used to identify a significant discontinuity in linear growth rates, and nonlinear regression indicated that the negatively accelerating growth rates characteristic of postnatal growth in general were not maintained during the period of accelerated growth during puberty.

A factor restricting comparison of studies is uncertainty in age designation. An age designated as 1 year could be equivalent to 365 days (determined on a day basis) or 336 days (based on 12 4-week months). Similarly, it is not clear whether an age stated in months is based on the number of calendar months (for example, February 15 to May 15), the number of 4-week months, or the the portion of the year (1/12 of 365 days). Such uncertainties could reconcile or offset comparisons made by as much as 60 days. It would be preferable to use fractions of years, based on a 365 day year, for such assessments.

There has been discussion in the literature concerning the uniqueness of the human adolescent growth spurt among primate species (Laird, 1967; Bogin, 1988). Our quantitative analysis, along with that of others (Watts and Gavan, 1982; German et al., 1994), supports the occurrence of an adolescent growth spurt in female macaque monkeys. Comparison of pubertal growth across primate species must be tempered by consideration of maturation rates, differences in sex differentiation of body size and composition, and seasonality. In the case of female rhesus monkeys, such comparisons are difficult because of the imposition of seasonal patterns on reproductive maturation. Female rhesus typically reach menarche during the breeding season of their third year and first ovulate during the breeding season of their fourth year. Thus, growth patterns associated with sexual maturation in female rhesus could be distributed differently than in humans while having similar biological basis and significance.

In conclusion, these data suggest that a period of accelerated weight gain preceding menarche can be identified in a heterogeneous group of colony-reared rhesus monkeys. During this period, weight gain approximately doubles from the previous rate. Estimates of timing and extent of accelerated weight gain obtained from cross-sectional and longitudinal data are compatible.

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